UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

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MEMORANDUM

SUBJECT: Review of Atrazine Incident Reports
DP Barcode D270014, Chemical #080803

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BACKGROUND

The following data bases have been consulted for the poisoning incident data on the active ingredient Atrazine (PC Code:080803):

1) OPP Incident Data System (IDS) - reports of incidents from various sources, including registrants, other federal and state health and environmental agencies and individual consumers, submitted to OPP since 1992. Reports submitted to the Incident Data System represent anecdotal reports or allegations only, unless otherwise stated. Typically no conclusions can be drawn implicating the pesticide as a cause of any of the reported health effects. Nevertheless, sometimes with enough cases and/or enough documentation risk mitigation measures may be suggested.

2) Poison Control Centers - as the result of a data purchase by EPA, OPP received Poison Control Center data covering the years 1993 through 1996 for all pesticides. Most of the national Poison Control Centers (PCCs) participate in a national data collection system, the Toxic Exposure Surveillance System which obtains data from about 65-70 centers at hospitals and universities. PCCs provide telephone consultation for individuals and health care providers on suspected poisonings, involving drugs, household products, pesticides, etc.

3) California Department of Pesticide Regulation - California has collected uniform data on suspected pesticide poisonings since 1982. Physicians are required, by statute, to report to their local health officer all occurrences of illness suspected of being related to exposure to pesticides. The majority of the incidents involve workers. Information on exposure (worker activity), type of illness (systemic, eye, skin, eye/skin and respiratory), likelihood of a causal relationship, and number of days off work and in the hospital are provided.

4) National Pesticide Telecommunications Network (NPTN) - NPTN is a toll-free information service supported by OPP. A ranking of the top 200 active ingredients for which telephone calls were received during calendar years 1984-1991, inclusive has been prepared. The total number of calls was tabulated for the categories human incidents, animal incidents, calls for information, and others.

ATRAZINE REVIEW

I. Incident Data System

Please note that the following cases from the IDS do not have documentation confirming exposure or health effects unless otherwise noted.

Incident#113-1

A pesticide incident occurred in 1992, when a man's neighbor sprayed a corn field with the product. The next day the wind blew the product onto his yard and the man reported a severe headache. No further information on the disposition of the case was reported.

Incident#302-9

A pesticide incident occurred in 1992, when an individual was exposed to the product dermally and reported cellulitis and a rash. No

further information on the disposition of the case was reported.

Incident#302-20
A pesticide incident occurred in 1992, when an individual was exposed to the product dermally and reported skin irritation. No further information on the disposition of the case was reported.

Incident#636-11
A pesticide incident occurred in 1985, when a company sprayed a nearby area with atrazine. A nearby pond is used by the landowner for back water for the well. After it rains, the well water causes the man's wife and daughter to become sick. No further information on the disposition of the case was reported.

Incident#999-59
A pesticide incident occurred in 1994, when an individual reported a rash and fasciculations. No further information on the disposition of the case was reported.

Incident#1148-1
A pesticide incident occurred in 1994, when a man applied the product in a T-shirt, shorts, and tennis shoes and reported red welts and ringing of his ears. No further information on the disposition of the case was reported.

Incident#1189-2
A pesticide incident occurred in 1994, when an individual reported a rash, dermal irritation, and pain. No further information on the disposition of the case was reported.

Incident#1189-13
A pesticide incident occurred in 1993, when an individual reported pruritus, ocular irritation and pain, and a dry eye sensation. No further information on the disposition of the case was reported.

Incident#1192-116
A pesticide incident occurred in 1994, when an individual reported a dermal rash. No further information on the disposition of the case was reported.

Incident#1263-1
A pesticide incident occurred in 1994, when one case was exposed through the ocular route and reported ocular irritation and pain. A second case was exposed through the oral route and reported dermal

irritation and pain, oral irritation, edema, and pruritus. No further information on the disposition of the case was reported.

Incident#2984-1

A pesticide incident occurred in 1995, when a woman, who has a history of allergies and exercise asthma and is a smoker, was hospitalized for experiencing asthma for five days after applying the product. She applied the product while using a dust mask. She visited her physician due to her coughing and was later treated and released. About three days later, she went back to her physician and was admitted to the hospital. No further information on the disposition of the case was reported.

Incident#3068-7

A pesticide incident occurred in 1995, when an individual was exposed through the dermal route and reported diarrhea, confusion, renal failure, and dehydration. No further information on the disposition of the case was reported.

Incident#3471-8

A lawsuit involved a plaintiff who reported burn injuries after exposure to atrazine.

Incident#4616-1

A pesticide incident occurred in 1996, when the product was applied to 40 acres of corn in a preplant application. The field is located across the road from a man's property who reported a rash, swollen forehead, and difficulty breathing. He was treated by a physician for an allergic reaction. No further information on the disposition of the case was reported.

Incident#4697-10

A lawsuit involved a plaintiff who reported shoulder discomfort, arthritis, nodules in the arm, and general pain. The plaintiff's neighbor applied the product along a fence line that bordered the two properties.

Incident#4697-21

A lawsuit involved a plaintiff who reported nausea and diarrhea after some well water was contaminated.

Incident#4697-51

A lawsuit involved a plaintiff who reported chronic conjunctivitis, blurred vision, and scarring after working as a transit authority signalman.

Incident#4697-64
A lawsuit involved a plaintiff who reported hypersensitivity and dizziness after pesticide was sprayed on a yard.

Incident#4697-78
A lawsuit involved a plaintiff who reported neurological problems after the chemical was used to treat soil.

Incident#5895-1
A pesticide incident occurred in 1996, when an adult and child were exposed to spray drift and reported blurred vision, burning eyes, pressure in chest, infant not sleeping, drainage from nose, and a temperature. No further information on the disposition of the case was reported.

Incident#5895-2
A pesticide incident occurred in 1994, when an individual reported nausea after they were exposed to the product by inhalation while adding water to a tank. No further information on the disposition of the case was reported.

Incident#5895-3
A pesticide incident occurred in 1992, when an individual reported cardiac arrest after their neighbor's house was treated with the product. No further information on the disposition of the case was reported.

Incident#5895-4
A pesticide incident occurred in 1995, when an individual reported burning sensations all over their body after being sprayed with the product. No further information on the disposition of the case was reported.

Incident#5895-5
A pesticide incident occurred in 1996, when an individual reported burning and itching on their hands, face, arms, and throat and a strange taste in the mouth. No further information on the disposition of the case was reported.

Incident#5895-6
A pesticide incident occurred in 1992, when an individual reported eye irritation, blurred vision, and pain in the bony part of the eyes after the product got into their eyes. No further information on the disposition of the case was reported.

Incident#5895-7
A pesticide incident occurred in 1992, when an individual got the product into their eyes. They reported eye irritation and redness and soreness around the eye lids. No further information on the disposition of the case was reported.

Incident#5895-29
A pesticide incident occurred in 1993, when an individual was accidentally sprayed with the product. They reported difficulty breathing and a skin rash. No further information on the disposition of the case was reported.

Incident#5895-31
A pesticide incident occurred in 1995, when an individual cleaned up a spill and drank well water. They reported headaches. No further information on the disposition of the case was reported.

Incident#5895-32
A pesticide incident occurred in 1996, when an individual cleaned out a sprayer and reported hives and skin lesions. No further information on the disposition of the case was reported.

Incident#5895-33
A pesticide incident occurred in 1996, when an individual walked through treated seed. They reported welts and blisters on the body and a sore throat. No further information on the disposition of the case was reported.

Incident#5895-34
A pesticide incident occurred in 1992, when an individual reported a rapid heartbeat. No further information on the disposition of the case was reported.

Incident#5895-35
A pesticide incident occurred in 1992, when an individual reported memory loss after they inhaled the product. No further information on the disposition of the case was reported.

Incident#5895-38
A pesticide incident occurred in 1992, when an individual applied the product and reported tachycardia. No further information on the disposition of the case was reported.

Incident#5895-39
A pesticide incident occurred in 1994, when an individual reported

a salty taste in the mouth and a burning face after the product was spilled in the basement. No further information on the disposition of the case was reported.

Incident#6880-3

A pesticide incident occurred in 1989, when a man, who is an applicator, reported dizziness and burning skin after he loaded a terragator. No further information on the disposition of the case was reported.

Incident#6880-4

A pesticide incident occurred in 1989, when a man applied the product and reported muscle spasms and ataxia. No further information on the disposition of the case was reported.

Incident#6880-9

A pesticide incident occurred in 1992, when a man applied the product and reported nausea, anorexia, and fatigue. No further information on the disposition of the case was reported.

Incident#6880-19

A pesticide incident occurred in 1994, when a man, who was not wearing gloves, unloaded drums of the product and reported swollen and red hands. No further information on the disposition of the case was reported.

Incident#7314-1

A pesticide incident occurred in 1998, when a two and a half gallon container leaked and a truck driver was exposed to the product. He reported a burning sensation in his eyes. No further information on the disposition of the case was reported.

Incident#7644-27

A pesticide incident occurred in 1998, when a worker reported blisters between the fingers and bumps on his hands. No further information on the disposition of the case was reported.

Incident#7690-5

A pesticide incident occurred in 1998 that resulted in a minor effect. No further information on the disposition of the case was reported.

Incident#7690-9

A pesticide incident occurred in 1998 that resulted in a minor

effect. No further information on the disposition of the case was reported.

Incident#7962-1

A lawsuit involved a plaintiff who reported burns to his skin and eyes as a result of aerial over spray of the product to a field adjacent to his home. Seven months later he was diagnosed with metastatic lung cancer and later died. No further information on the disposition of the case was reported.

Incident#9019-49

A pesticide incident occurred in 1999, when a woman applied the product on her lawn and reported an extreme rash on her arm. She was treated by a physician for her symptoms. No further information on the disposition of the case was reported.

Incident#9548-1

A pesticide incident occurred in 1999, when an individual, who worked at an atrazine packaging plant for four years, reported short-term memory loss for several months. No further information on the disposition of the case was reported.

II. Poison Control Center Data - 1993 through 1998

Results for the years 1993 through 1998 are presented below for occupational cases, non-occupational involving adults and older children, and for children under age six. Cases involving exposures to multiple products are excluded. Tables 1-4 present the hazard information for atrazine compared with all other pesticides on six measures: percent with symptoms, percent with moderate, major, or fatal outcome, percent with major or fatal outcome, percent of exposed cases seen in a health care facility, and percent hospitalized and percent seen in a critical care facility. Table 1 reports the number of cases on which the data derived in Tables 2-4 are based. Table 2 presents this information for occupational cases, Table 3 for non-occupational cases involving adults and older children (six years or older), and Table 4 for children under age six.

Table 1. Number of atrazine exposures reported to the Toxic Exposure Surveillance System (AAPCC), number with determined outcome, number

seen in a health care facility for occupational and non-occupational cases (adults and children six years and older) and for children under six years of age only, 1993-1998 .

Subgroup	Exposures	Outcome determined	Seen in Health Care Facility
Occupational: adults and older children	75	33	28
Non-occupational: adults and older children	186	78	59
Children under age six	64	25	6

Table 2. Comparison between atrazine and all pesticides for percent cases with symptomatic outcome (SYM), moderate or more severe outcome (MOD), life-threatening or fatal outcome (LIFE-TH), seen in a health care facility (HCF), hospitalized (HOSP), or seen in an intensive care unit (ICU) reported to Poison Control Centers, 1993-1998 for occupational cases only.

Pesticide	SYM*	MOD*	LIFE-TH*	HCF*	HOSP*	ICU*
Atrazine	90.9%	12.1%	0%	37.3%	14.28%	3.57%
All Pesticides	86.0%	18.8%	0.62%	47.3%	7.18%	2.85%
Ratio	1.06	0.64	0.00	0.79	1.99	1.25

* Symptomatic cases based on those cases with a minor, moderate, major, or fatal medical outcome. Denominator for SYM, MOD, and LIFE-TH is the total cases where medical outcome was determined. Denominator for HCF is all exposures. Denominator for HOSP and ICU is all cases seen in a health care facility.

Table 3. Comparison between atrazine and all pesticides for percent cases with symptomatic outcome (SYM), moderate or more severe outcome (MOD), life-threatening or fatal outcome (LIFE-TH), seen in a health

care facility (HCF), hospitalized (HOSP), or seen in an intensive care unit (ICU) reported to Poison Control Centers, 1993-1998 for non-occupational cases involving adults and older children.

Pesticide	SYM*	MOD*	LIFE-TH*	HCF*	HOSP*	ICU*
Atrazine	66.7%	16.7%	1.28%	31.7%	11.9%	3.39%
All Pesticides	68.5%	10.5%	0.36%	18.1%	7.35%	3.24%
Ratio	0.97	1.59	3.56	1.75	1.61	1.05

* Symptomatic cases based on those cases with a minor, moderate, major, or fatal medical outcome. Denominator for SYM, MOD, and LIFE-TH is the total cases where medical outcome was determined. Denominator for HCF is all exposures. Denominator for HOSP and ICU is all cases seen in a health care facility.

Table 4. Comparison between atrazine and all pesticides for percent cases with symptomatic outcome (SYM), moderate or more severe outcome (MOD), life-threatening or fatal outcome (LIFE-TH), seen in a health care facility (HCF), hospitalized (HOSP), or seen in an intensive care unit (ICU) for adults and children six years and older reported to Poison Control Centers, 1993-1998 for children under six years old..

Pesticide	SYM*	MOD*	LIFE-TH*	HCF*	HOSP*	ICU*
Atrazine	36.0%	8.00%	0%	9.4%	0%	0%
All Pesticides	21.8%	1.40%	0.12%	16.8%	5.12%	1.48%
Ratio	1.65	5.71	0.00	0.56	0.00	0.00

* Symptomatic cases based on those cases with a minor, moderate, major, or fatal medical outcome. Denominator for SYM, MOD, and LIFE-TH is the total cases where medical outcome was determined. Denominator for HCF is all exposures. Denominator for HOSP and ICU is all cases seen in a health care facility.

For occupational cases atrazine appears to have less hazard of moderate or major effects. However, there were four cases hospitalized and one seen in a critical care facility that resulted in higher than average requirements for health care. Non-occupational cases showed greater evidence of hazard with higher percentages of cases with moderate and major effects as well as requirements for health care and

hospitalization. Note that the excess reported for major effects is based on a single case that reportedly had cardiac arrest and coma. It is not clear from the information on this case why the symptoms were so severe. Examination of cases reporting moderate effects did not show any consistent pattern of reported signs or symptoms and no cases similar to the one major case. This suggests that at least some of the cases had coincidental or unrelated effects to their exposure.

For cases involving children under six years of age, atrazine exposure was more likely to result in minor or moderate symptoms. But it should be noted this was based on relatively few cases, seven children with minor symptoms and two children with moderate symptoms. Dermal and ocular effects accounted for the majority of symptoms associated with exposure to atrazine, though a significant number of cases also reported gastrointestinal, neurological, and respiratory effects.

III. California Data - 1982 through 1996

Detailed descriptions of one case submitted to the California Pesticide Illness Surveillance Program (1982-1996) were reviewed. In the case, a worker used the product to contribute to production of a commodity. Specific symptoms were not mentioned.

IV. National Pesticide Telecommunications Network

On the list of the top 200 chemicals for which NPTN received calls from 1984-1991 inclusively, atrazine was ranked 33rd with 117 incidents in humans reported and 28 incidents in animals (mostly pets).

V. Literature Review

No significant literature citations were found concerning poisoning incidents due to atrazine. There are a number of cancer epidemiology studies of atrazine or triazine herbicides as a group, a number of which have been previously reviewed by HED. Reviews of cohort studies conducted at manufacturing plants are listed here:

1. Blondell, Jerome. September 13, 1996. Review of Two Atrazine Epidemiology Studies (DP Barcode D226645). Memorandum to Kathryn Boyle.

This review covers "A Follow-up Study of Workers at the Ciba-Geigy St. Gabriel Plant" by Elizabeth Delzell, Ilene Brill, and Colleen Beall, completed April 8, 1996 (MRID no. 440086-01) and "Atrazine: an Epidemiological Study at the Schweizerhalle Plant" by R. Gass and G. A. Stalder completed on January 15, 1993 (MRID No. 440086-02). A number of earlier reviews have been completed for earlier versions of the first study:

2. Blondell, Jerome. January 22, 1990. Ciba-Geigy Triazine Herbicide Mortality Study (HED Project No. 0-224). Memorandum to Lois Rossi.

3. Blondell, Jerome. July 15, 1994. Review of Retrospective Triazine Mortality Studies (DP barcode 189027). Memorandum to Walt Waldrop.

4. Allen, Ruth. July 11, 1996. OREB Epidemiology Review and Recommendations for the Special Review of Atrazine (DP Barcode 215496). Memorandum to Joe Bailey.

HED concluded that neither of the epidemiologic studies reviewed add significant new information concerning adverse health effects of atrazine. A non-significant elevation in non-Hodgkin's lymphoma continues to be observed at the Louisiana plant among workers exposed to triazines, including atrazine. By itself, this study does not support a conclusion of increased cancer from exposure to triazines. However, this study could be considered supportive, but only supportive and not definitive, if evidence of an association between non-Hodgkin's lymphoma and triazine exposure was available from other studies. Follow-up by the National Cancer Institute in four states looked specifically to determine whether earlier associations in individuals studies could be attributed to atrazine when adjustment was made for exposures to other pesticides. They concluded that "detailed analyses suggested that there was little or no increase in the risk of NHL attributable to the agricultural use of atrazine" (Zahm et al. 1993). The Health Effects Division concurs with this finding.

In addition to these studies, a number of retrospective epidemiology studies have been published and reviewed by HED, which are listed below:

1. Blondell, Jerome. September 21, 1990. Italian Triazine Cancer Epidemiology Studies, HED Project No. 0-1573. Memorandum to Jude Andreason.
This review covers two articles by Donna et al. “Ovarian mesothelial tumors and herbicides: a case-control study”. Carcinogenesis 5:941-942, 1984 and “Triazine herbicides and ovarian epithelial neoplasms”.

Scandinavian Journal of Work, Environment and Health 15:47-53, 1989.

2. Blondell, Jerome. February 14, 1991. Review of midwest cancer epidemiology studies related to triazines. HED Project No. INTRA-0141. Memorandum to Henry Spencer.

This review covers the following studies:
- Hoar SK, Blair A, Holmes FF, Boysen CD, Robel RJ, Hoover R, Fraumeni, Jr. JF. 1986. Agricultural herbicide use and risk of lymphoma and soft-tissue sarcoma. Journal of the American Medical Association 256:1141-1147.

- Brown LM, Blair A, Gibson R, Everett GD, Cantor KP, Schuman LM, Burmeister LF, Van Lier SF, Dick F. 1990. Pesticide exposures and other agricultural risk factors for leukemia among men in Iowa and Minnesota. Cancer Research 50:6585-6591.

- Hoar SK, Blair A, Holmes FF, Boysen C, Robel RJ. 1985. Herbicides and colon cancer (letter to the editor). Lancet 1 (8440):1277-1278.

- Zahm SH, Weisenburger DD, Babbitt PA, Saal RC, Cantor KP, Blair A. 1988. A case-control study of non-Hodgkin's lymphoma and agricultural factors in Eastern Nebraska. American Journal of Epidemiology 128:901.

- Cantor K, Everett G, Blair A, Gibson R, Schuman L, Isacson P. 1985. Farming and non-Hodgkins's lymphoma (Meeting Abstract). American Journal of Epidemiology 122:535-536.

This review concluded in part:

> The study by Hoar et al. (1985) of colon cancer and the study by Brown et al. (1990) of leukemia did not find a significant association between cancer and triazine exposure. The Kansas study of Non-Hodgkin's lymphoma (NHL) by Hoar et al. (1986) found a significant association for triazines (odds ratio = 2.5, 95 % confidence interval 1.2-5.4) which was not studied in detail because the main focus of the study was phenoxy herbicide exposure. A follow-up study in Nebraska found a risk of 1.4 (confidence interval 0.8-2.2) which was not significant but did show evidence of increasing with duration of use (odds ratio with 16 or more years of use was 2.0). The study in Iowa and Minnesota by Cantor et al. (1985) found an elevated risk of small cell lymphocytic lymphoma associated with use of atrazine (odds ratio = 1.6, confidence interval not given) and cyanazine (odds ratio = 1.6, confidence interval not given). This last study, however, is only available in abstract form and insufficient detail is

available to evaluate the apparent elevation in risk. The Louisiana plant study submitted by Ciba-Geigy previously reviewed found one NHL death and one NHL incident case which provide suggestive evidence of an association.

Detailed summary of key studies

Provided below are more detailed summaries of the two key studies specific to atrazine.

Role of the herbicide atrazine in the development of non-Hodgkin's lymphoma

Zahm et al. (1993) combined three population-based case-referent studies from Nebraska, Iowa-Minnesota, and Kansas to evaluate the role of atrazine in the development of NHL. The studies in Iowa-Minnesota and Kansas included white men, and in Nebraska, the study included both white men and women. In Nebraska, the study involved 227 white men, twenty-one years or older who had been diagnosed with NHL between July 1, 1983 and June 30, 1986. In Iowa-Minnesota, the study involved 780 white men, thirty years or older who were newly diagnosed cases with the disease between March 1981 and October 1983, and in Minnesota between October 1980 and September 1982. In Kansas, the study involved 200 white men, twenty-one years or older between 1979 and 1981. Controls were randomly selected from the same geographic areas as the cases and were matched by race, gender, five-year age groups, and vital status. An odds ratio of 1.4 was determined for the three studies combined for 101 NHL and 214 controls where atrazine was used on farms where they worked or lived. The odds ratio ranged from 1.2 in Iowa to 2.7 in Kansas. In two of the states and in all states combined, the risks were higher for farmers who used atrazine in their farming operations but did not handle the chemical than among farmers who handled atrazine. Other than atrazine, the farmers could have been exposed to other herbicides and insecticides which could have increased their chances of experiencing NHL. The study concluded that there “was little or no increase in the risk of NHL attributable to the agricultural use of atrazine”.

A Review of Epidemiologic Studies of Triazine Herbicides and Cancer Ciba-Geigy Triazine Herbicide Mortality Study

On November 22, 1989, a mortality study of workers at a triazine herbicide manufacturing plant was received from Ciba-Geigy Corporation, for review by the Health Effects Division. In St. Gabriel, Louisiana, in 1970, the plant started operating which manufactured atrazine, simazine, and propazine. A cohort of 1,472 workers were identified who worked for at least 6 months in the plant and were involved in

production activities that would result in exposure. Vital status was determined for 99 percent of this cohort as of January 1, 1987. Death certificates were obtained on all 13 decedents and classified according to international (ICD) disease codes. Mortality in the cohort was compared with the general population of the U.S. and Louisiana using the Standardized Mortality Ratio (SMR). The SMR is defined as the observed number of deaths due to a particular cause divided by the expected number, multiplied by 100. The overall expected number of deaths was 28. Given only 13 observed deaths, this yields an SMR of 46 with a 95 percent confidence interval of 24 to 78, a significant deficit. No significant excess of deaths were reported for any disease category. The SMR for cancer was 82 based on 3 observed deaths and 3.7 expected.

The one concern raised in this study was the report of one death from NHL in a worker with five years of experience at the plant who died at age 31, and another worker who was diagnosed with NHL in 1986 (still alive) who started working at the plant in 1970. The one death is not statistically significant, however the two cases of NHL (while the study does not say so explicitly) could be considered a significant excess morbidity. The age of the case diagnosed in 1986 should have been reported.

VI. Conclusions

From the review of the Incident Data System, it appears that a majority of cases involved skin illnesses such as dermal irritation and pain, rashes, and welts and eye illnesses such as eye damage, blurred vision, conjunctivitis, irritation, and pain. Poison Control Center data tend to support the Incident Data System results, dermal and ocular effects were the most common effects reported due to occupational exposure.

VII. Recommendations

Appropriate protective clothing to protect the skin and eyes of handlers and field workers is recommended. For workers who may have extensive exposure to atrazine, skin protection should be required.

cc: Correspondence
Atrazine file (chemical no. 080803)
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